



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 December 2018
EMA/661289/2018

Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector containing a bioengineered capsid and a codon-optimised expression cassette to drive the expression of the SQ form of a B-domain deleted human coagulation factor VIII for the treatment of haemophilia A

On 26 October 2018, orphan designation (EU/3/18/2079) was granted by the European Commission to Spark Therapeutics Ireland Limited, Ireland, for recombinant adeno-associated viral vector containing a bioengineered capsid and a codon-optimised expression cassette to drive the expression of the SQ form of a B-domain deleted human coagulation factor VIII (also known as SPK-8011) for the treatment of haemophilia A.

What is haemophilia A?

Haemophilia A is an inherited bleeding disorder that is caused by the lack of factor VIII, which is one of the proteins involved in the blood coagulation (clotting) process. Patients with haemophilia A are prone to bleeding and bleed for a long time after injury or surgery. Bleeding can also happen within muscles or in the joints, such as the elbows, knees and ankles. This can lead to permanent injury if it happens repeatedly.

Haemophilia A is a debilitating disease that is life long and may be life threatening because bleeding can occur in the brain, spinal cord or gut.

What is the estimated number of patients affected by the condition?

At the time of designation, haemophilia A affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).



What treatments are available?

At the time of designation, medicines containing factor VIII were authorised in the EU for the treatment of haemophilia A, to replace the missing protein. However, factor VIII medicines did not work in some patients with haemophilia A because the immune system (the body's natural defences) can produce 'inhibitors' (antibodies) against factor VIII which stop the factor VIII medicine from working. In these cases, different blood clotting factors or other treatments needed to be used, either alone or as part of a combination treatment.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with haemophilia A because preliminary results indicate that it can improve the levels of factor VIII circulating in the blood in the long term.

This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Patients with haemophilia A cannot make enough functioning factor VIII because the gene for producing the clotting factor is damaged.

This medicine is made of a virus that contains normal copies of the gene responsible for producing factor VIII. When injected into the patient's vein, it is expected that the virus will be carried into the liver cells and start producing factor VIII. It is expected that a single dose of the medicine will maintain raised levels of factor VIII for a long time thereby reducing bleeding.

The type of virus used in this medicine ('adeno-associated virus') does not cause disease in humans.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial with the medicine in patients with haemophilia A was ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for haemophilia A. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 September 2018 recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant adeno-associated viral vector containing a bioengineered capsid and a codon-optimised expression cassette to drive the expression of the SQ form of a B-domain deleted human coagulation factor VIII	Treatment of haemophilia A
Bulgarian	Рекомбинантен адено-асоцииран вирусен вектор, съдържащ обработен по биотехнологичен метод капсид и кодон-оптимизирана експресионна касета на SQ формата на човешки коагулационен фактор VIII с отстранен B-домейн	Лечение на хемофилия А
Croatian	Rekombinantni adeno-povezani virusni vektor koji sadrži bioinženjeringom dobiveni kapsid i ekspresijsku kasetu optimiziranu kodonom da se potakne ekspresija SQ oblika humanog faktora VIII koagulacije s deletiranom B-domenom	Liječenje hemofilije A
Czech	Rekombinantní adeno-asociovaný virový vektor obsahující bioinženýrovanou kapsidovou a kodonově optimalizovanou expresní kazetu pro řízení exprese SQ formy lidského koagulačního faktoru VIII majícího B-doménu	Léčba hemofilie A
Danish	Rekombinant adenoassocieret viral vektor indeholdende en bioengineeret kapsid og kodonoptimeret ekspressionskassette til at drive ekspresionen af SQ-formen af en B-domæne-slettet human koagulationsfaktor VIII	Behandling af hæmofili A
Dutch	Recombinant adeno-geassocieerde viral vector welke een bio-gemanipuleerd capsid en een codon-geoptimaliseerd expressie-cassette bevat, om de uitdrukking te drijven van de SQ vorm van een humane coagulatiefactor VIII met verwijderd B- domein	Behandeling van hemofilie A
Estonian	Rekombinantne adeno-assotsieerunud viirusvektor, mis sisaldab biotehnoloogilist kapsiidi ja koodon-optimeeritud ekspresioonikassetti eesmärgiga stimuleerida inimese deleteerunud B-domeeniga hüübimisfaktori VIII SQ vormi ekspressiooni	Hemofiilia A ravi
Finnish	Rekombinantti adenoassosioitu virusvektori, joka sisältää bioteknologisen kapsidin ja kodonioptimoidun ekspressiokasetin aikaansaaden hyytymistekijä VIII:n (B-domaani poistettu) SQ-muodon ekspression	Hemofilia A:n hoito
French	Vecteur viral adeno-associé recombinant qui contient une capsid et une cassette d'expression codon optimisé pour former l'expression de la forme SQ du domaine B éliminée du facteur de coagulation humaine VIII	Traitement de l'hémophilie A

¹ At the time of designation

Language	Active ingredient	Indication
German	Rekombinanter adeno-assoziiertes-Virus-Vektor umfassend ein durch Biotechnik erzeugtes Kapsid und eine Codon-optimierte Expressionskassette, um die Expression der SQ-Form eines B-Domänen-deletierten menschlichen Koagulationsfaktors VIII zu fördern	Behandlung der Hämophilie A
Greek	Ανασυνδυασμένος αδeno-σχετιζόμενος ιικός φορέας που περιέχει ένα βιομηχανικά τροποποιημένο καψίδιο και μία κασέττα έκφρασης βελτιστοποιημένων κωδικονίων για την έκφραση του SQ τύπου ενός ανθρώπινου παράγοντα πήξης VIII με αφαιρεμένη την περιοχή B	Θεραπεία της αιμορροφιλίας A
Hungarian	Biomérnöki úton előállított kapszidot és egy kodon-optimalizált expressziós kazettát tartalmazó rekombináns adenoasszociált vírusvektor, mely egy B-domén-törölt human koagulációs factor VIII SQ formájának expresszióját vezérli	A típusú hemofília kezelése
Italian	Vettore virale adeno-associato ricombinante contenente un capsid bioingegnerizzato e una cassetta di espressione con codon ottimizzato per l'espressione della forma SQ del fattore VIII della coagulazione umana senza dominio B	Trattamento dell'emofilia A
Latvian	Rekombinants adeno-asociētais virālais vektors, kas satur bioinženierētu kapsīdu un ekspresijas kaseti ar optimizētu kodonu, lai vadītu cilvēka koagulācijas faktora VIII ar B-domēna delēciju SQ formas ekspresiju	A tipa hemofilijas ārstēšana
Lithuanian	Rekombinantinis su adeno virusu susijęs vektorius, turintis bioinžinerijos būdu sukurtą kapsidę ir pagal kodonus suderinta raiškos kasetė žmogaus krešėjimo faktoriaus VIII su B domeno delecija SQ formos raiškai	Hemofilijos A gydymas
Maltese	Vettur virali adeno-assoċjat li fih capsid b'inginerija bijoloġika rekombinanti u każett ta' espressjoni tal-codon li jkun ottimizzat biex jagħti spinta lill-espressjoni tal-formola VIII SQ ta' fattur tad-dominju B tal-koagulazzjoni umana li tithassar	Kura ta' l-emofilja A
Polish	Rekombinowany związany z adenowirusami wektor wirusowy zawierający bioinżynieryjnie zmodyfikowany kapsyd oraz kasetę ekspresyjną ze zoptymalizowanymi kodonami, która eksprymuje formę SQ ludzkiego czynnika VIII krzepnięcia z usuniętą domeną B	Leczenie hemofilii A
Portuguese	Vetor viral adeno-associado recombinante contendo um capsíde de bioengenharia e uma cassete de expressão com codão otimizado para a expressão da forma SQ do fator VIII da coagulação humana deletado do domínio B	Tratamento da hemofilia A
Romanian	Vector viral recombinant adeno-asociat ce conține o capsidă obținută prin bioinginerie și o casetă de expresie codon-optimizată pentru a declanșa expresia formei SQ a factorului de coagulare uman VIII ce prezintă deleția domeniului B	Tratamentul hemofiliei A

Language	Active ingredient	Indication
Slovak	Rekombinantný adeno-asociovaný vírusový vektor obsahujúci kapsid a kodón-optimalizovanú exprimujúcu kazetu na vyvolanie expresie SQ formy B-domény vymazaného ľudského koagulačného faktora VIII	Liečba hemofílie A
Slovenian	Rekombinantni adeno-povezani virusni vektor, vsebujoč z bioinženiringom pridobljeno kapsido in ekspresijsko kaseto, optimizirano s kodonom za spodbujanje ekspresije SQ oblike koagulacijskega faktorja VIII z deletirano B-domeno	Zdravljenje hemofilije A
Spanish	Vector viral adenoasociado recombinante que contiene un capsido y casete de codon optimizado para fomentar la expresion de la forma SQ del dominio B deletido del factor de coagulacion humano VIII	Tratamiento de la hemofilia A
Swedish	Rekombinant adeno-associerad virusvektor innehållande en kapsid, tillverkad med bioteknik, och en kodonoptimerad utryckskasset för att driva uttrycket av SQ formen av B-domän delaterad human koagulationsfaktor VIII	Behandling av hemofili A
Norwegian	Rekombinant adenoassosiert virusvektor som koder for et syntetisert kapsid og en kodonoptimalisert ekspresjonskasset som driver ekspresjonen av SQ-formen av den humane koagulasjonsfaktoren VIII der B-domenet er slettet	Behandling av hemofili A
Icelandic	Raðbrigða adenoveirutengd genaferja sem inniheldur hjúp sem hannaður er með erfðaverkfræði og tjáningarstæðu af tákni sem hefur verið magnað til að knýja áfram tjáningu SQ forma af manna storkupætti VIII með eyddu B-hneppi	Meðferð við dreypasýki A